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NYHA functional class I, and MR severity by TEE (assessed by an independent core-lab) has remained mild (**Figure 1**, Online Video 3) with an EROA = 0.09 cm^2 and RVol = 12 ml/beat.

Transcatheter therapies for treatment of cardiac diseases are increasingly being adopted, particularly for high-risk surgical patients. This case demonstrates the feasibility of percutaneous transseptal delivery of a "surgical-like" adjustable posterior annuloplasty Dacron band. Cardioband implantation was associated with substantial reduction of the septolateral annular dimension, to an extent comparable to that obtained by surgical annuloplasty. Clinical studies are warranted to appraise its risk-benefit balance in absolute terms and in comparison, or in combination, with other transcatheter mitral valve repair strategies.

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http://dx.doi.org/10.1016/j.jcin.2014.08.003

Please note: This work was supported by Valtech Cardio Ltd, Or Yehuda, Israel. Dr. Maisano is a consultant for Valtech Cardio, Abbott Vascular, Medtronic, and St. Jude Medical; and has received royalties from Edwards Lifesciences. Dr. Latib is on the advisory board of Medtronic; and is a consultant for Direct Flow Medical, Valtech Cardio, and 4-Tech Cardio. Dr. Denti and Andrea Guidotti are consultants for Valtech Cardio. Drs. La Canna, Kuck, Colombo, Alfieri, and Messika-Zeitoun have received research grants from Valtech Cardio. Dr. Vahanian has received research grants from Valtech Cardio; and is on the advisory boards of Valtech Cardio and Abbott. Dr. Taramasso has reported that he has no relationships relevant to the contents of this paper to disclose.

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APPENDIX For the supplemental videos, please see the online version of this article.

Experience With an Innovative New Food and Drug Administration Pathway for First-in-Human Studies

Carotid Baroreceptor Amplification for Resistant Hypertension

It has now been over 2 years since *JACC: Cardiovascular Interventions* published the Bertog et al. state-of-the-art review (1) "Renal Denervation for Hypertension," detailing the physiological rationale for renal denervation (RDN) in resistant hypertension. Since then, interest in the field of sympathetic modulation soared exponentially but was quickly brought back to earth with the publication of the SYMPLICITY HTN-3 (Renal Denervation in Patients With Uncontrolled Hypertension) study, the only blinded, randomized study of RDN, which failed to meet its pre-specified efficacy endpoint (2). It is currently unclear whether the results of SYMPLICITY-3 were due to technically inadequate ablation, underestimation of additional benefits from study-mediated medical therapy, or inappropriate patient selection, or whether the initial hypothesis was in some way flawed. We believe the former issues are likely in play and that the optimistic conclusions from Bertog et al. (1) for RDN will ultimately hold true. However, given the unmet need of alternative therapeutic options for resistant hypertension, exploration for alternative methods to modulate sympathetic tone is warranted.

It is well known that the carotid baroreflex is an important feedback loop for hemodynamic balance and adrenergic tone. Carotid baroreceptors are known to activate by pulsatile stretch rather than pressure and the receptor response decays when stimulation from stretch is constant, explaining why hemodynamic changes after carotid stenting are generally transient (3). A study of electrical baroreceptor stimulation for treatment of resistant hypertension via a surgical implant adjacent to the carotid sinus was successful in lowering blood pressure (BP), however, it did not meet its pre-specified procedural safety endpoint (4). Although effective, this surgical risk may not be acceptable for most resistant hypertensive patients. Combining knowledge of baroreceptor physiology with known pressure-strain relationships for pressurized tubular structures, we hypothesized that certain geometric changes of the carotid bulb

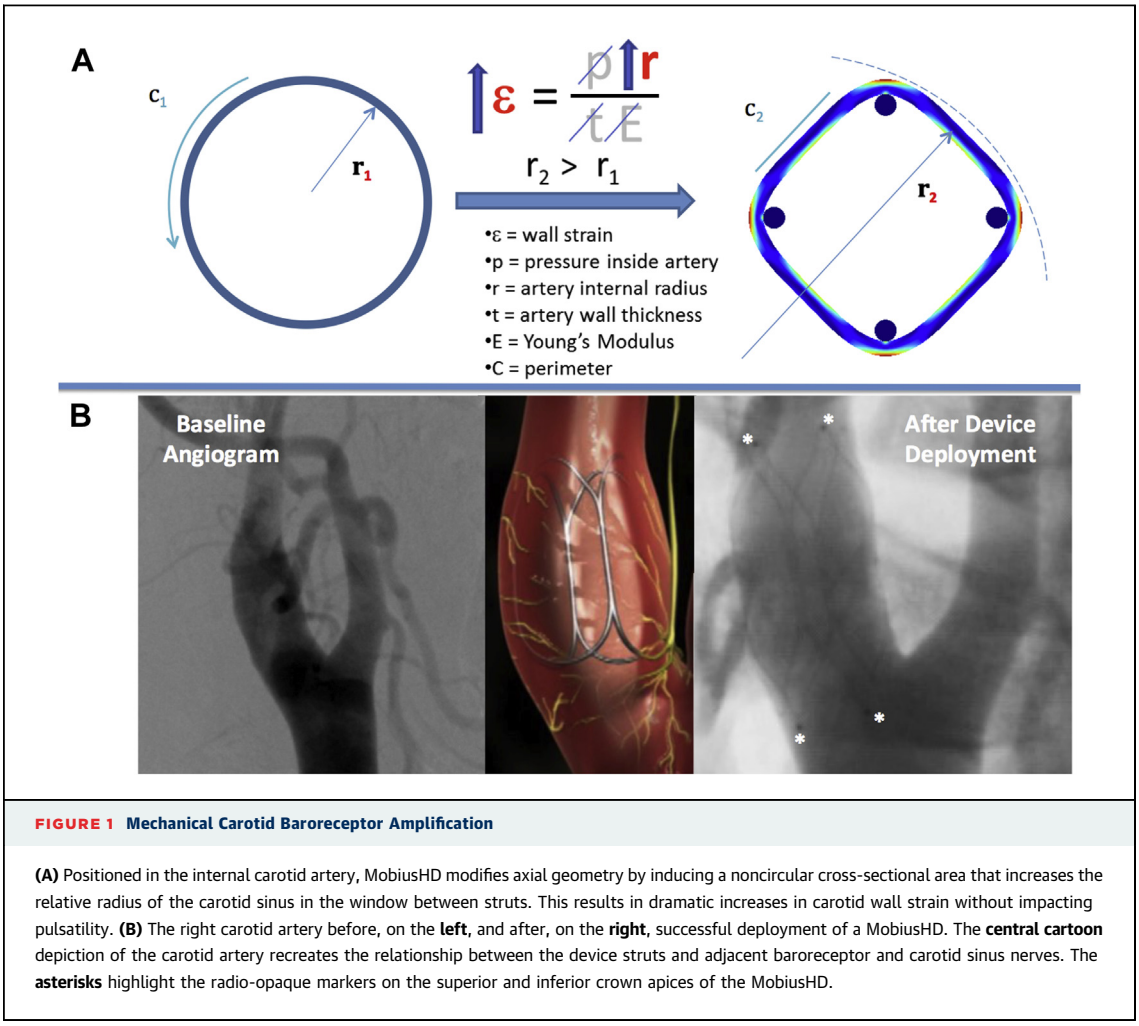

FIGURE 1 Mechanical Carotid Baroreceptor Amplification

(A) Positioned in the internal carotid artery, MobiusHD modifies axial geometry by inducing a noncircular cross-sectional area that increases the relative radius of the carotid sinus in the window between struts. This results in dramatic increases in carotid wall strain without impacting pulsatility. **(B)** The right carotid artery before, on the **left**, and after, on the **right**, successful deployment of a MobiusHD. The **central cartoon** depiction of the carotid artery recreates the relationship between the device struts and adjacent baroreceptor and carotid sinus nerves. The **asterisks** highlight the radio-opaque markers on the superior and inferior crown apices of the MobiusHD.

can create sustainable amplification of baroreceptor feedback. This theory led to development of an intravascular prosthesis that alters carotid bulb geometry with the intent of increasing wall stretch. Specifically, the device increases the relative radius of the carotid sinus in the window between struts (Figure 1) resulting in dramatic increases in carotid bulb strain. Subsequent extensive pre-clinical studies, finite element flow analysis, and animal and cadaveric studies led to approval for a first-in-human study by the United States Food and Drug Administration (FDA) Early Feasibility Medical Device Clinical Studies Program (IDE#G130013) entitled the CALM-FIM_US (Controlling and Lowering Blood Pressure With the MobiusHD) study. This study was 1 of 9 studies to be approved for this novel FDA pathway, and we believe this program reflects a positive and noteworthy change in the bureaucratic landscape for U.S. innovation. The fast-track model allowed us to perform the first-in-human case in the United States before the mirror European protocols could be initiated.

The first-in-human case was performed following approval by the Emory University Institutional Review Board and involved a 56-year-old African-American man with a 30-year history of hypertension, type 2 diabetes mellitus, obesity, and a negative workup for secondary hypertension. He had failed to respond to an optimally dosed stable regimen of 5 antihypertensive agents, including amlodipine, carvedilol, lisinopril, hydralazine, and furosemide. His BP was monitored daily at home for 2 weeks during an initial screening period, with a mean value of 159/99 mm Hg. This 2-week period included medication adherence monitoring via medication diary and daily self-recording of BP. An office based BP measurement after the 2-week screening period was 164/93 mm Hg, with a baseline heart rate of 57 beats/min. Duplex ultrasound and magnetic resonance angiography performed in preparation for carotid

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baroreflex sensitivity did not reveal carotid atherosclerosis. Carotid massage testing demonstrated no evidence of hypersensitivity, and orthostatic maneuvers demonstrated normal response.

Carotid angiography confirmed the absence of atherosclerosis and pre-specified carotid size parameters compatible with the study device. The device was placed without incident using standard of care carotid stenting techniques (**Figure 1**). Given the minimal embolic risk, distal embolic protection was not utilized to avoid unnecessary vascular perturbation. No acute changes were noted in either BP or heart rate during the procedure, and the patient's neurological status was stable.

The patient was observed overnight with a discharge BP the following morning of 125/75 mm Hg. Heart rate remained unchanged from baseline values at 61 beats/min. Between 1 and 6 months following his procedure, the patient recorded daily home BP readings with a mean of 133/86 mm Hg (range 107 to 159 mm Hg/66 to 101 mm Hg). He had no evidence of neurological alteration, and at his most recent follow-up visit (217 days post-procedure), his office BP demonstrated a sustained reduction to 138/74 mm Hg. The patient reports excellent health with no clinical adverse events. Temporal trends in office-based BP measurements, home BP measurements, and 24-h ambulatory BP monitoring from screening to 217 days post-procedure also showed improvement. Follow-up duplex ultrasound imaging of the ipsilateral carotid artery revealed stable device position and no evidence of trauma, stenosis, or elevated velocities within the treated vessel.

The CALM-FIM study is a safety study planning to enroll 20 patients in the United States and 20 in Europe. The risk-benefit analysis and subsequent pivotal trial design will need to address the inherent risk of carotid arterial access and concerns regarding placement of a chronic implant in this vessel. However, the new FDA pathway for this type of complex potential innovation hopefully represents a positive change in the bureaucratic milieu.

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http://dx.doi.org/10.1016/j.jcin.2014.07.009

Please note: Dr. Devireddy has served on an Advisory Board of Medtronic. Dr. Bates is a consultant for Vascular Dynamics, but has received no reimbursement for conducting the clinical trial or for conduct of the study; and is a consultant for CeloNova BioSciences; and is also a shareholder in unrelated agreements with CeloNova BioSciences and Nexeon MedSystems.

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